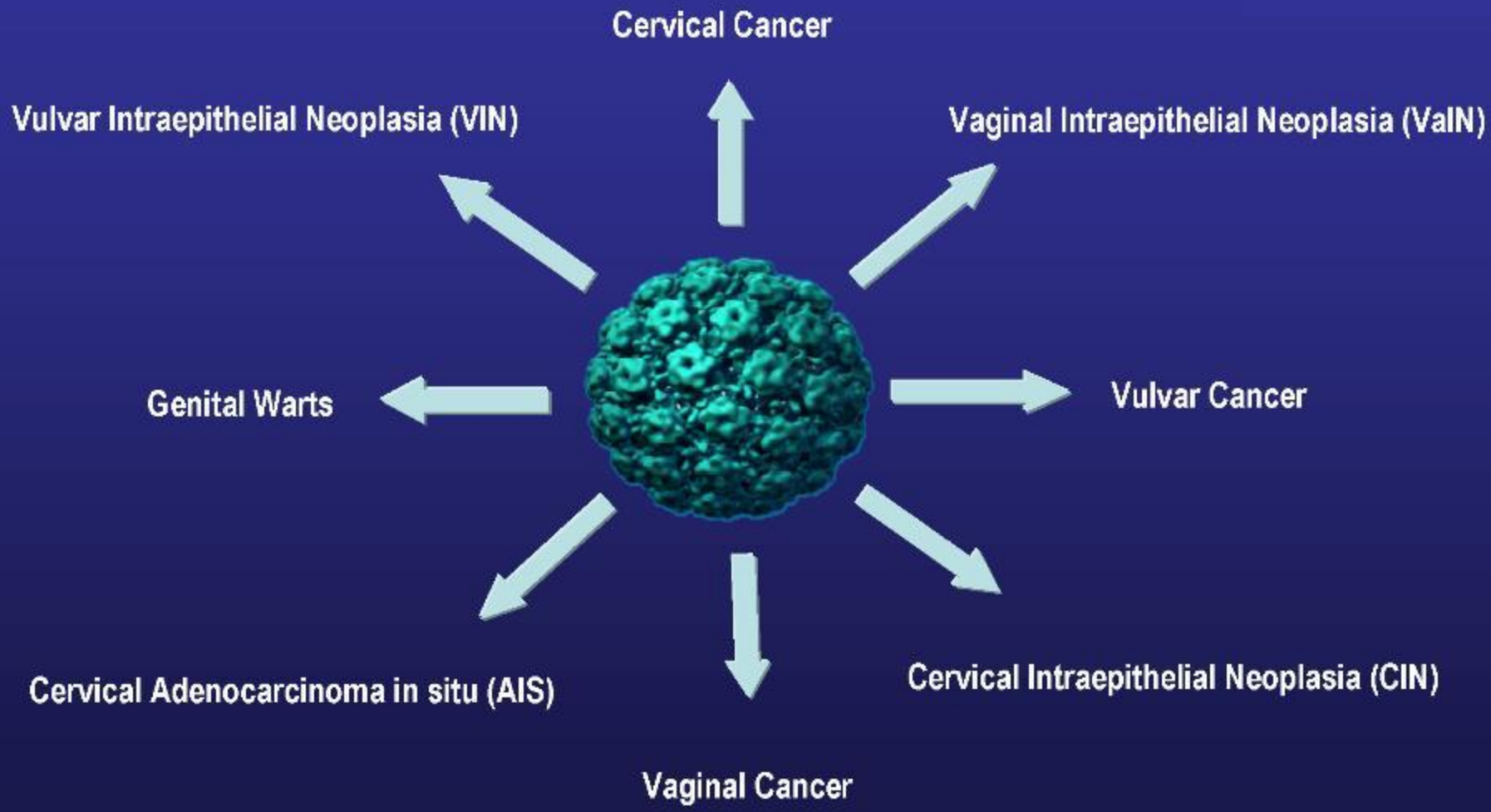
Human Papillomavirus (HPV)

Burden of Infection and Associated Pathologies

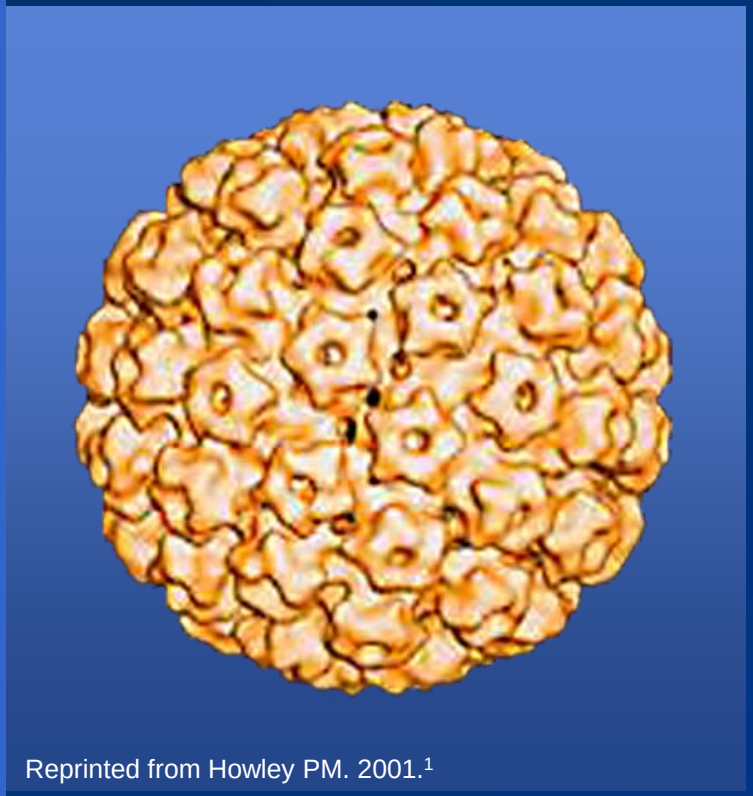
HPV Is Associated With Many Conditions[1]



1. Braaten KP et al. *Rev Obstet Gynecol.* 2008;1(1):2–10.

HPV

Nonenveloped double-stranded DNA virus[1]



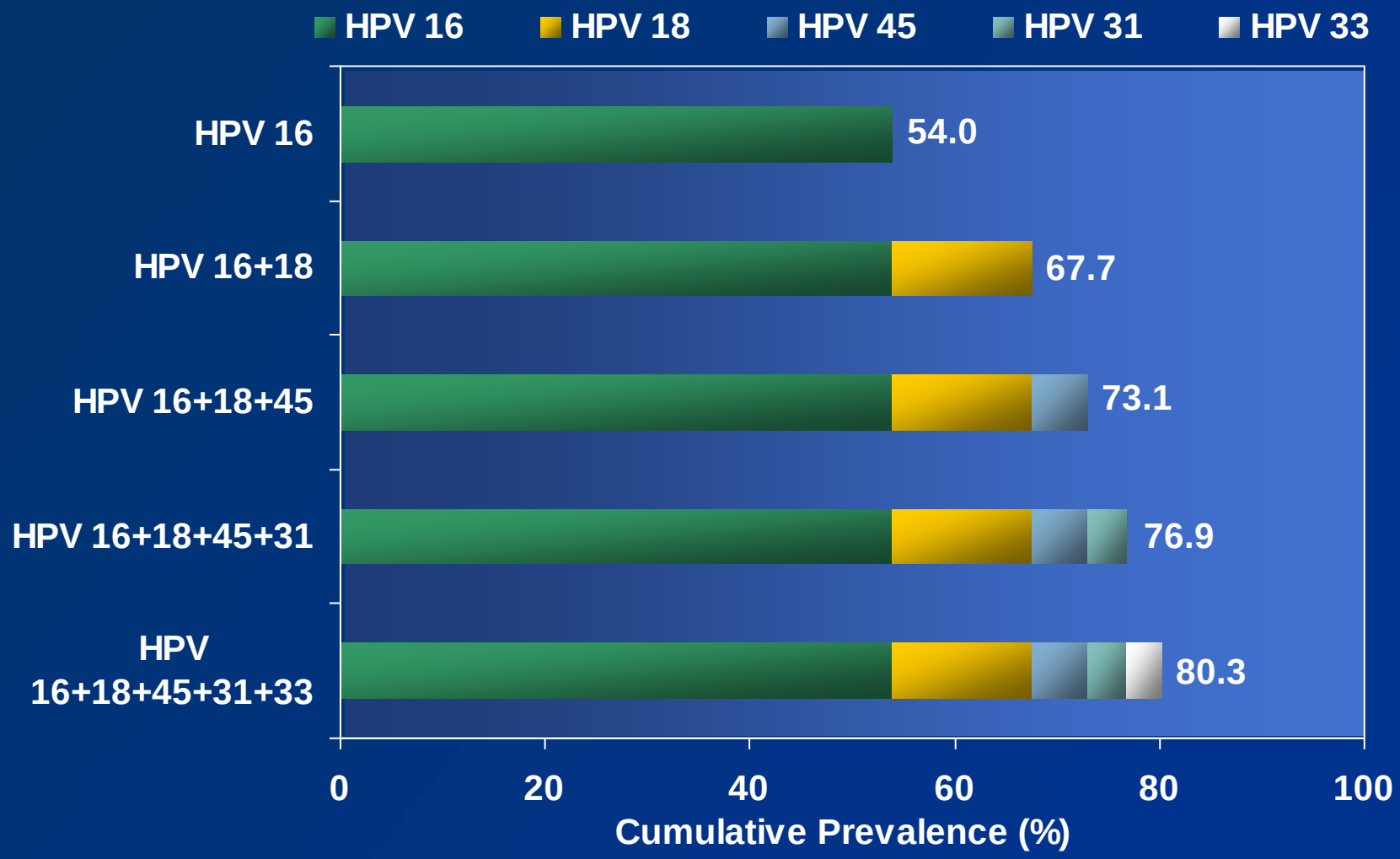
Reprinted from Howley PM. 2001.[1]

- >100 types identified[2]
- 30–40 anogenital[2,3]
  - 15–20 oncogenic*[,2,3] types, including 16, 18, 31, 33, 35, 39, 45, 51, 52, 58[4]
    - HPV 16 (54%) and HPV 18 (13%) account for the majority of worldwide cervical cancers.[5]
  - Nononcogenic† types include: 6, 11, 40, 42, 43, 44, 54[4]
    - HPV 6 and 11 are most often associated with external anogenital warts.[3]

*High risk; †Low risk

1. Howley PM. In: Fields BN, Knipe DM, Howley PM, eds. *Fields Virology.* 4th ed. Philadelphia, Pa: Lippincott-Raven; 2001:2197–2229. Reprinted with the permission of Lippincott-Raven. 2. Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934. 3. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis*. 2002;35(suppl 2):S210–S224. 4. Muñoz N, Bosch FX, de Sanjosé S, et al. *N Engl J Med*. 2003;348:518–527. 5. Clifford GM, Smith JS, Aguado T, Franceschi S. *Br J Cancer*. 2003:89;101–105.

Most Common HPV Types in Cervical Cancer: Cumulative Prevalence (Squamous Cell Carcinoma)[1]



1. Bosch FX, de Sanjosé S. *J Natl Cancer Inst Monogr*. 2003;31:3–13.

HPV and Cancer: A Broader Picture[1]

Cancer	% Associated With Certain HPV Types
Cervical*	≥95%
Vaginal*	50%
Vulvar*	>50%
Penile	50%
Anal	>70%
Oropharyngeal	20%
Nonmelanoma skin/cutaneous squamous cell	90%†

*Includes cancer and intraepithelial neoplasia
†Immunocompromised patients

1. González Intxaurraga MA, Stankovic R, Sorli R, Trevisan G. *Acta Dermatovenerol.* 2002;11:1–8.

US HPV Statistics

- Lifetime risk for sexually active men and women is at least 50%.[1]
  - By 50 years of age, at least 80% of women will have acquired genital HPV infection.[1]
- Estimated incidence: 6.2 million per year[1]
- Estimated prevalence: 20 million[2]
- In sexually active individuals 15–24 years of age, ~9.2 million are currently infected.[3]
  - An estimated 74% of new HPV infections occur in this age group.[3]
  - In studies of women <25 years of age, prevalence rates ranged from 28% to 46%.[4,5]

1. Centers for Disease Control and Prevention. Rockville, Md: CDC National Prevention Information Network; 2004. 2. Cates W Jr, and the American Social Health Association Panel. *Sex Transm Dis*. 1999;26(suppl):S2–S7. 3. Weinstock H, Berman S, Cates W Jr. *Perspect Sex Reprod Health*. 2004;36:6–10. 4. Burk RD, Ho GYF, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis*. 1996;174:679–689. 5. Bauer HM, Ting Y, Greer CE, et al. *JAMA*. 1991;265:472–477.

HPV Is Easily Transmitted and Often Asymptomatic

Mechanisms of HPV Transmission and Acquisition

- Sexual contact
  - Through sexual intercourse[1]
    - Including anal intercourse
  - Genital–genital, manual–genital, oral–genital[2–4]
  - Genital HPV infection in virgins is rare, but may result from nonpenetrative sexual contact.[2]
  - If used correctly, condoms can help reduce the risk of HPV infection. However, the level of protection from HPV infection with condom use has not yet been determined.[5]
- Nonsexual routes
  - Mother to newborn (vertical transmission; rare)[6]
  - Fomites (eg, undergarments, surgical gloves, biopsy forceps)[7,8]
    - Hypothesized but not well documented
- Most infected individuals are unaware that they are infected and may unknowingly spread the virus.[9]

1. Kjaer SK, Chackerian B, van den Brule AJC, et al. *Cancer Epidemiol Biomarkers Prev*. 2001;10:101–106. **2.** Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. *Am J Epidemiol*. 2003;157:218–226. **3.** Fairley CK, Gay NJ, Forbes A, Abramson M, Garland SM. *Epidemiol Infect*. 1995;115:169–176. **4.** Herrero R, Castellsagué X, Pawlita M, et al. *J Natl Cancer Inst*. 2003;95:1772–1783. **5.** Centers for Disease Control and Prevention. Rockville, Md: CDC National Prevention Information Network; 2004. **6.** Smith EM, Ritchie JM, Yankowitz J, et al. *Sex Transm Dis*. 2004;31:57–62. **7.** Ferenczy A, Bergeron C, Richart RM. *Obstet Gynecol*. 1989;74:950–954. **8.** Roden RBS, Lowy DR, Schiller JT. *J Infect Dis*. 1997;176:1076–1079. **9.** Anhang R, Goodman A, Goldie SJ. *CA Cancer J Clin.* 2004;54:248–259.

Risk Factors for HPV Infection

Women

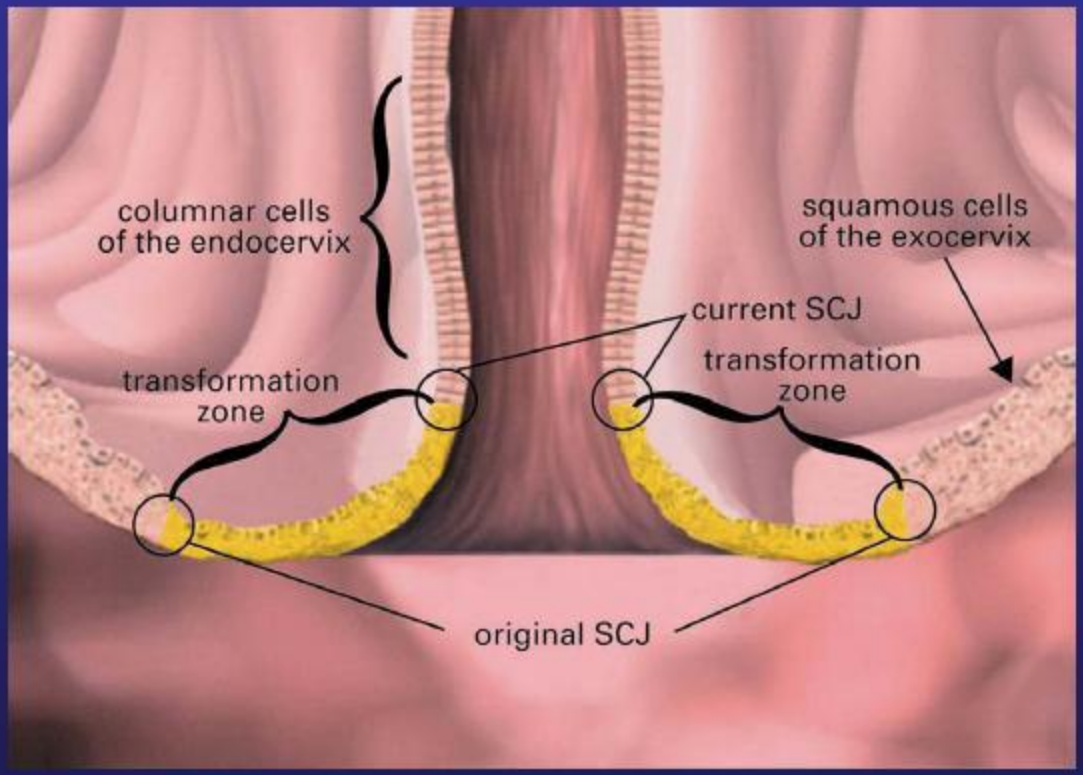
- Young age (peak age group 20–24 years of age)[1]
- Lifetime number of sex partners[2]
- Early age of first sexual intercourse[3]
- Male partner sexual behavior[3]
- Smoking[4]
- Oral contraceptive use[4]
- Uncircumcised male partners[5]

Men

- Young age (peak age group 25–29 years of age)[1]
- Lifetime number of sex partners[6]
- Being uncircumcised[6]

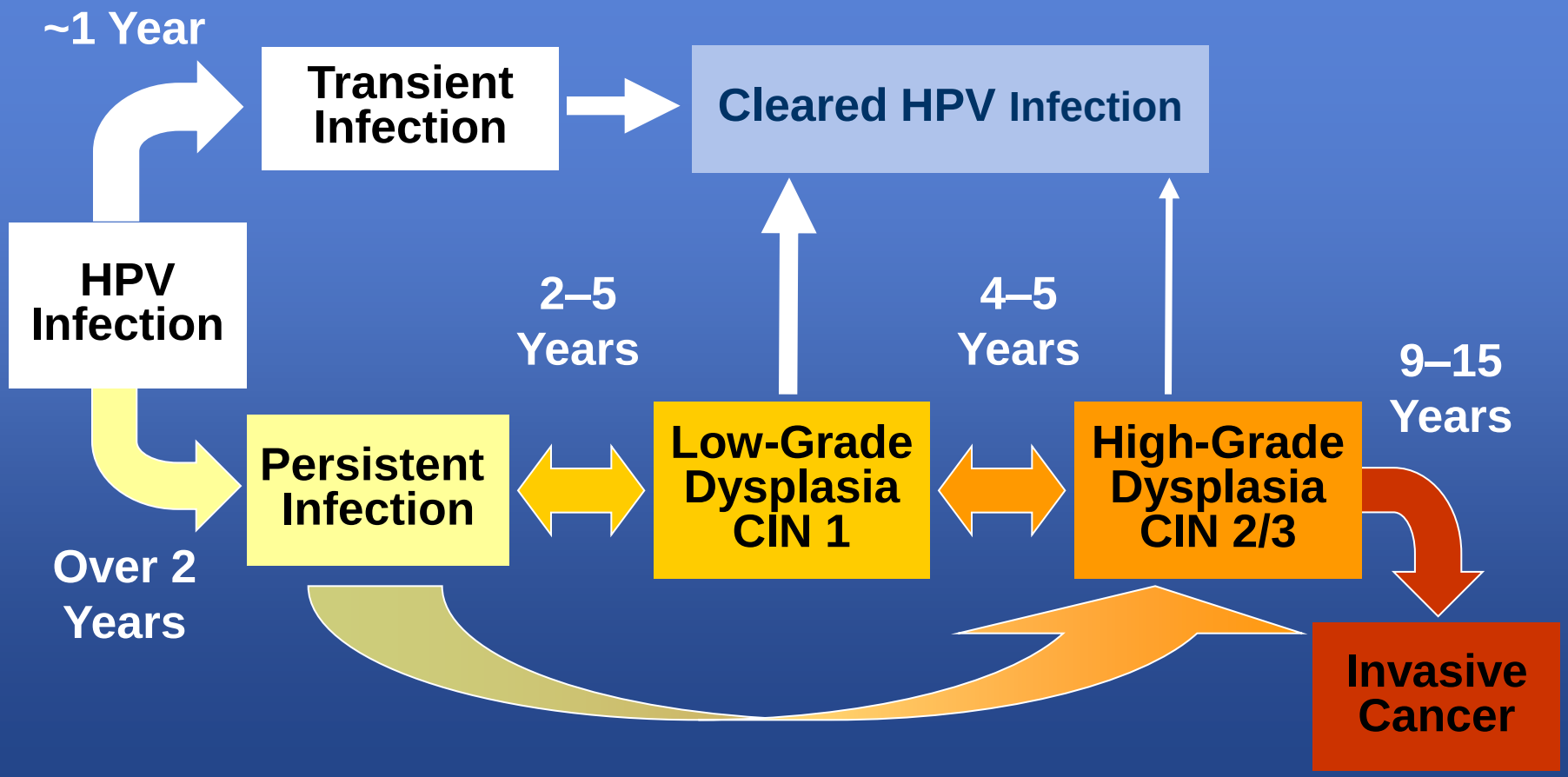
1. Insinga RP, Dasbach EF, Myers ER. *Clin Infect Dis.* 2003;36:1397–1403. 2. Burk RD, Ho GYF, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis*. 1996;174:679–689. 3. Murthy NS, Mathew A. *Eur J Cancer Prev*. 2000;9:5–14. 4. Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. *Am J Epidemiol*. 2003;157:218–226. 5. Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934. 6. Svare EI, Kjaer SK, Worm AM, Osterlind A, Meijer CJLM, van den Brule AJ. *Sex Transm Infect*. 2002;78:215–218.

The Cervical Transformation Zone



- Area of immature metaplasia between the original and current squamocolumnar junction (SCJ)
- ~99% of HPV-related genital cancers arise within the transformation zone of the cervix

Natural History of High-Risk HPV Infection and Potential Progression to Cervical Cancer[1,2]



Adapted from: 1. Pagliusi SR, Aguado MT. *Vaccine*. 2004;23:569–578. 2. Pinto AP, Crum CP. Clin Obstet Gynecol. 2000;43:352–362.

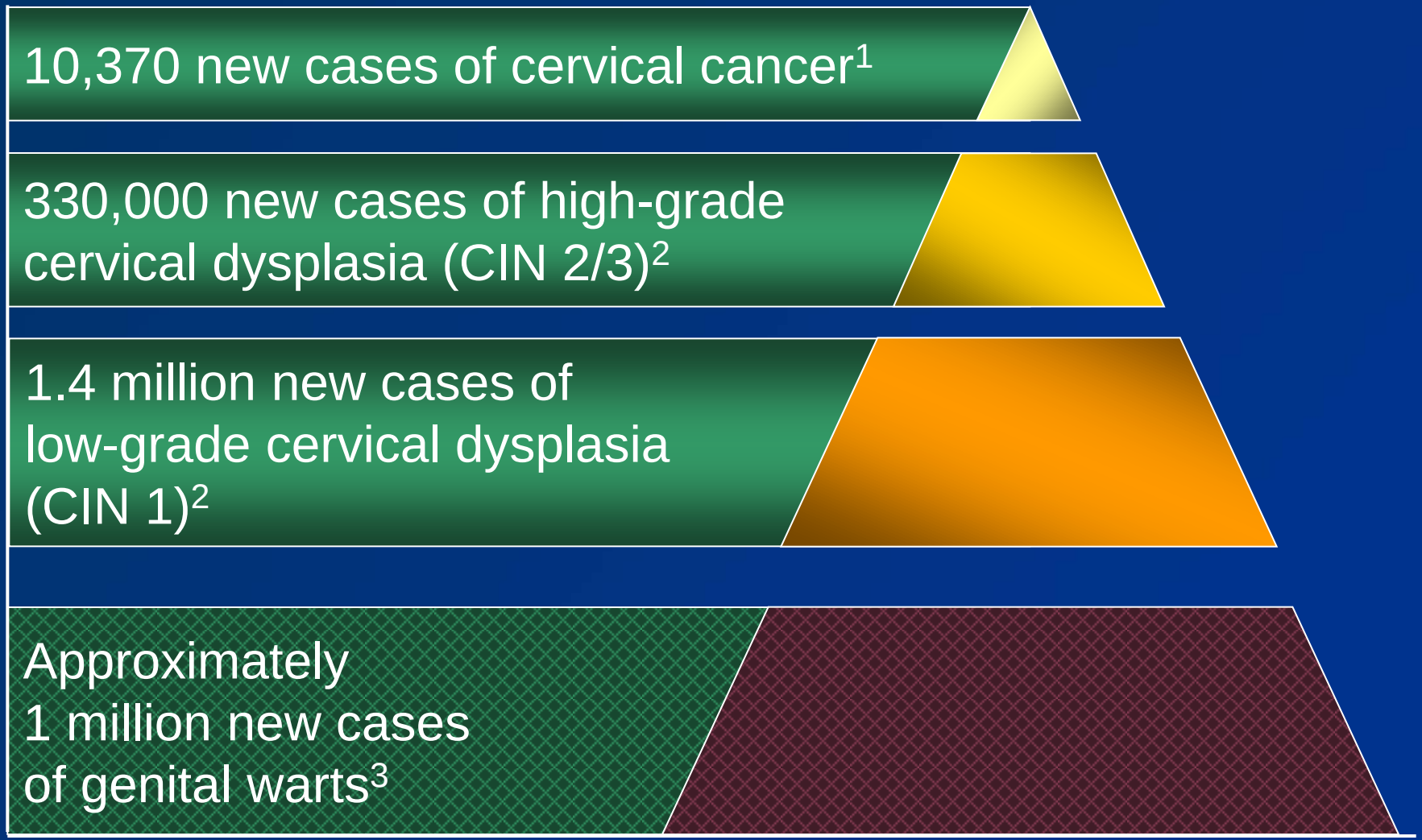
HPV Persistence

- Persistent infection: Detection of same HPV type two or more times over several months to 1 year[1]
- Widely accepted that persistence of high-risk types of HPV is crucial for development of cervical precancer and cancer[1]
- Other associated factors
  - Age (≥30 years)[*,2]
  - Infection with multiple HPV types[3]
  - Immune suppression[4]
- Currently, there are no antivirals available to treat the underlying HPV infection.[5]

*May be partially confounded by duration of infection

1. Schiffman M, Kjaer SK. *J Natl Cancer Inst Monogr*. 2003;31:14–19. 2. Hildesheim A, Schiffman MH, Gravitt PE, et al. *J Infect Dis.* 1994;169:235–240. 3. Ho GYF, Burk RD, Klein S, et al. *J Natl Cancer Inst.* 1995;87:1365–1371. 4. Kobayashi A, Greenblatt RM, Anastos K, et al. *Cancer Res*. 2004;64:6766–6774. 5. Stanley M. *J Natl Cancer Inst Monogr*. 2003;31:117–124.

Estimated Annual Incidence of Select HPV-Related Disease in the United States



1. American Cancer Society. *Cancer Facts & Figures 2005.* Atlanta, Ga: ACS; 2005:1−60. 2. Schiffman M, Solomon D. *Arch Pathol Lab Med.* 2003;127:946–949. 3. Fleischer AB, Parrish CA, Glenn R, Feldman SR. *Sex Transm Dis.* 2001;28:643–647.

Pap Smears: Benefits and Limitations

- Reduced cancer-causing mortality by more than two-thirds
- Pap smears, including conventional and thin-layer liquid based:
  - Relatively wide range of reported sensitivity, specificity, and positive predictive value[1–4]
  - Specific challenges for Pap smears include[2,5,6]:
    - Lack of sampling of lesions below the surface (they do not exfoliate)
    - Imperfect collection methods (some lesions are missed)
    - Inaccessibility of certain areas of the cervix
    - Errors of interpretation

1. Parham GP. *Am J Obstet Gynecol*. 2003;188:S13–S20. 2. Schink JC. *OBG Management.* 2003;(suppl):5–8. 3. Uyar DS, Eltabbakh GH, Mount SL. *Gynecol Oncol.* 2003;89:227–232. 4. Kulasingam SL, Hughes JP, Kiviat NB, et al. *JAMA*. 2002;288:1749–1757. 5. Selvaggi SM. *JAMA*. 2001;285:1506–1508. 6. Chacho MS, Mattie ME, Schwartz PE. *Cancer.* 2003;99:135–140.

HPV Clearance

- In women 15–25 years of age, ~80% of HPV infections are transient.[1]
  - Gradual development of cell-mediated immune response presumed mechanism[2]
- In a study of 608 college women, 70% of new HPV infections cleared within 1 year and 91% within 2 years.[3]
  - Median duration of infection = 8 months[3]
  - Certain HPV types are more likely to persist (eg, HPV 16 and HPV 18)

1. Meijer CJLM, Helmerhorst TJM, Rozendaal L, van der Linden JC, Voorhorst FJ, Walboomers JMM. *Histopathology*. 1998;33:83–86. 2. Schiffman M, Kjaer SK. *J Natl Cancer Inst Monogr*. 2003;31:14–19. 3. Ho GYF, Bierman R, Beardsley L, Chang CJ, Burk RD. *N Engl J Med*. 1998;338:423–428.

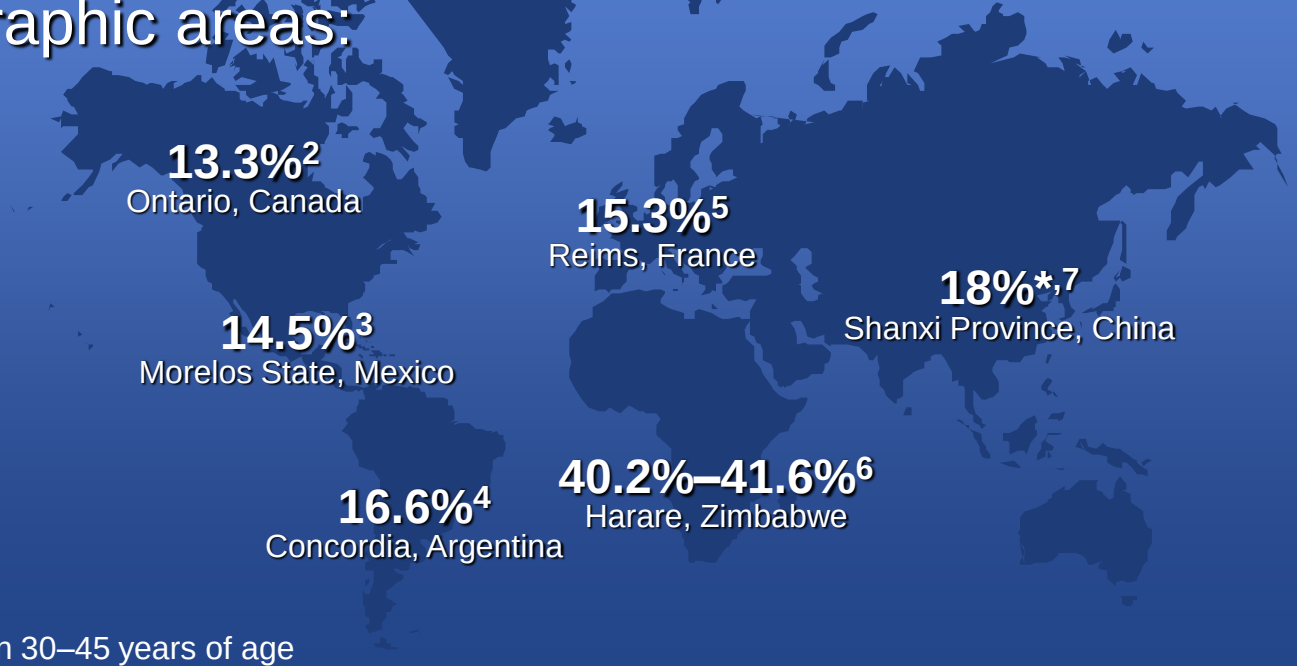
Biological Factors Increasing Susceptibility of Female Adolescents to HPV Infection

- Inadequate production of cervical mucus, which may act as a barrier against infection[1,2]
- Immature columnar epithelial cells in the transformation zone of the cervix are especially susceptible to HPV[1,2]
- Incomplete local immunity against certain infections[1,2]
- Increased susceptibility to minor trauma during sexual intercourse[1,2]

1. Kahn JA. *Curr Opin Pediatr*. 2001;13:303–309. 2. Rager KM, Kahn JA. *Curr Women Health Rep*. 2002;2:468–475.

Global HPV Statistics

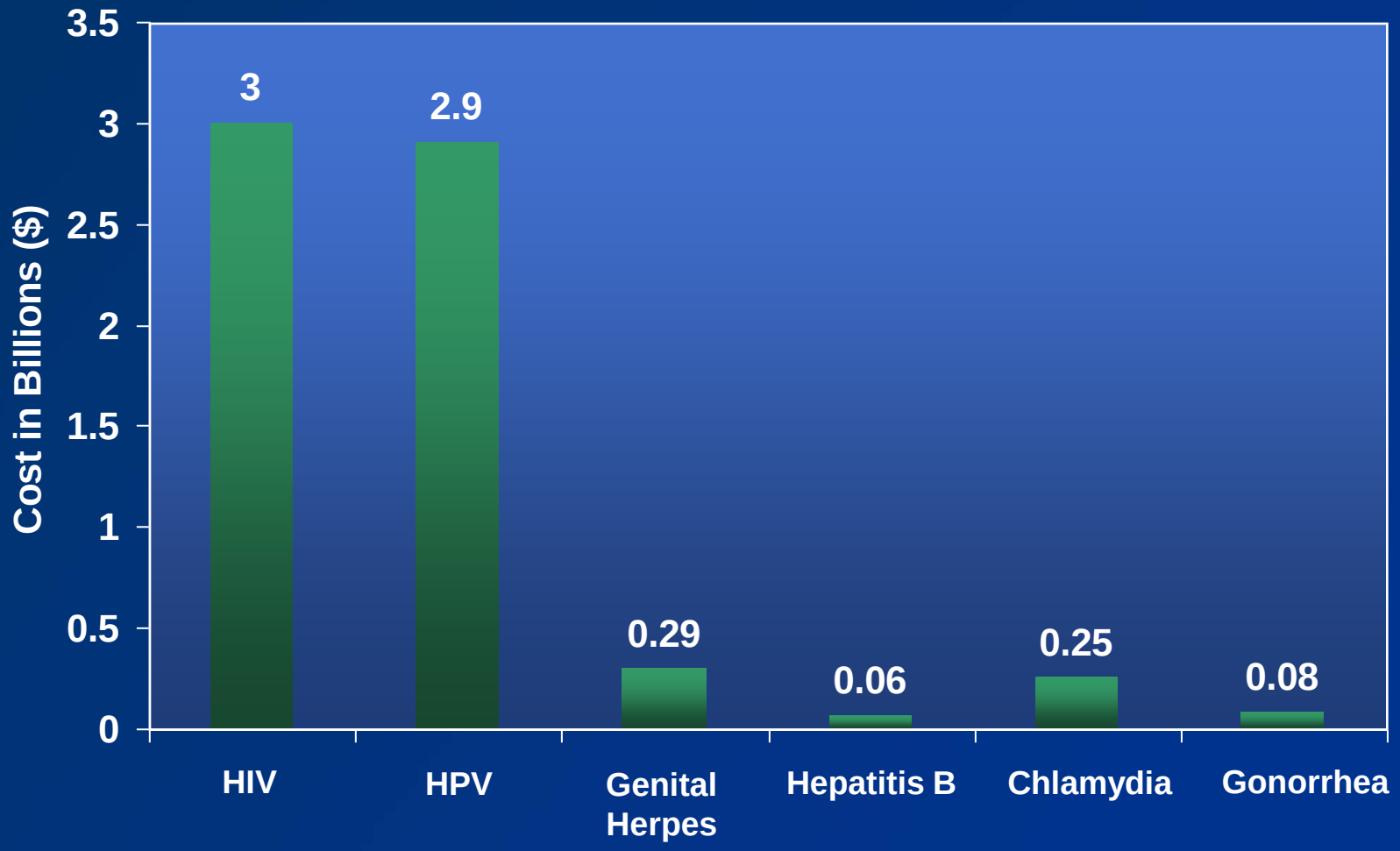
- Worldwide prevalence of HPV infection is estimated to be between 9% and 13%: ~630 million infected individuals.[1]
- Estimated prevalence of HPV infection in selected geographic areas:



*Among women 30–45 years of age

1. World Health Organization; 2001. Available at: http://www.who.int/vaccines/en/hpvrd/shtml. Accessed July 12, 2004. 2. Sellors JW, Mahony JB, Kaczorowski J, et al. *CMAJ*. 2000;163:503–508. 3. Lazcano-Ponce E, Herrero R, Muñoz N, et al. *Int J Cancer*. 2001;91:412–420. 4. Matos E, Loria D, Amestoy GM, et al. *Sex Transm Dis*. 2003;30:593–599. 5. Clavel C, Masure M, Bory JP, et al. *Br J Cancer*. 2001;84:1616–1623. 6. Blumenthal PD, Gaffikin L, Chirenje ZM, McGrath J, Womack S, Shah K. *Int J Gynecol Obstet*. 2001;72:47–53. 7. Belinson J, Qiao YL, Pretorius R, et al. *Gynecol Oncol*. 2001;83:439–444.

Estimated Direct Medical Costs of HPV and Other STIs in Persons 15–24 Years of Age, 2000[1]

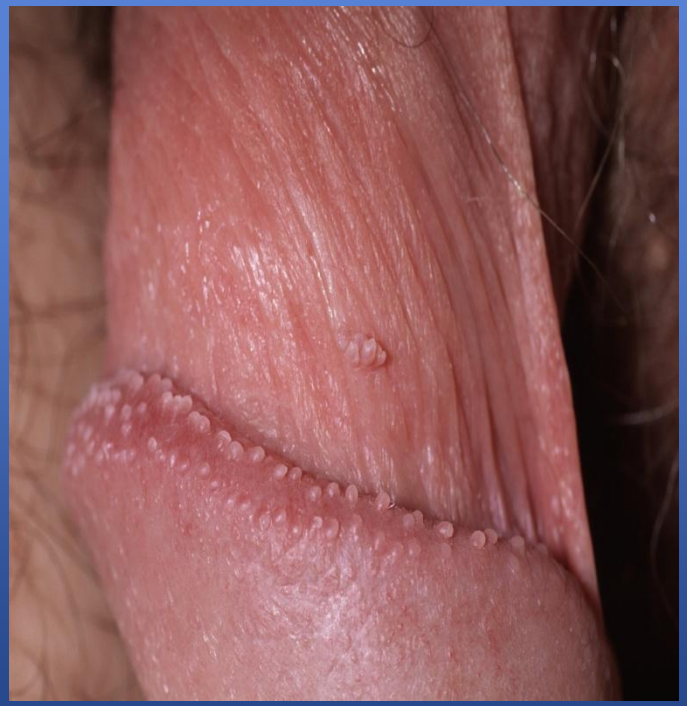


1. Chesson HW, Blandford JM, Gift TL, Tao G, Irwin KL. *Perspect Sex Reprod Health*. 2004;36:11–19.

HPV-Related Disease

- Anogenital Warts

HPV and Anogenital Warts

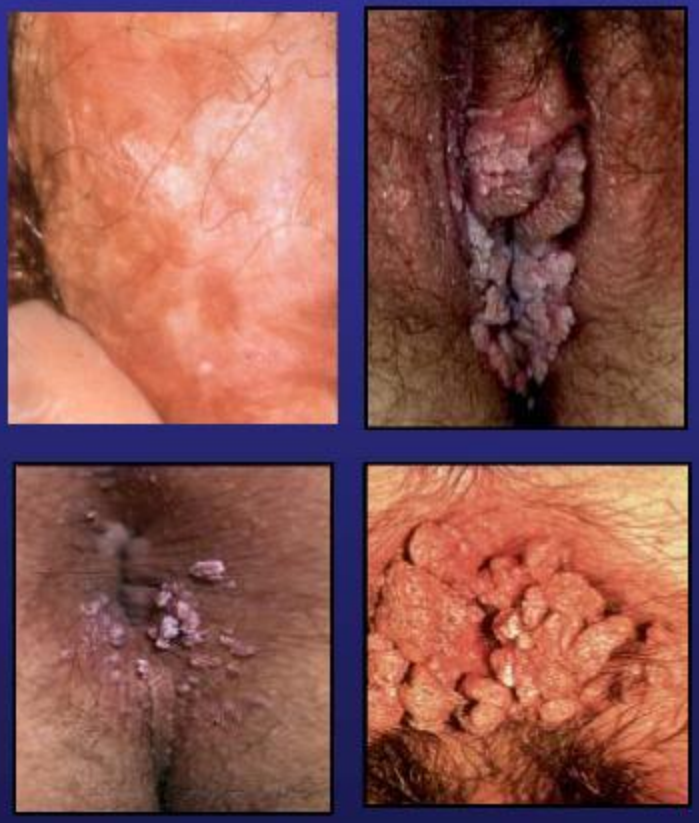


Genital warts

- HPV 6 and 11 responsible for >90% of anogenital warts[1]
- Infectivity >75%[2]
- Up to 30% spontaneously regress within 4 months.[3]
- Treatment can be painful and embarrassing.[4]
- Topical and surgical therapies are available for genital warts.[5]
- Recurrence rates vary greatly.[5]
  - As low as 5% with podofilox or laser treatment
  - As high as 65% with other treatments

1. Jansen KU, Shaw AR. Annu Rev Med. 2004;55:319–331. 2. Soper DE. In: Berek JS, ed. *Novak's* Gynecology. 13th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2002:453–470. 3. Lacey CJN. *J Clin Virol*. 2005;32(suppl):S82–S90. 4. Maw RD, Reitano M, Roy M. *Int J STD AIDS.* 1998;9:571–578. 5. Kodner CM, Nasraty S. *Am Fam Physician.* 2004;70:2335–2342.

Genital Warts: An Important Health care Issue



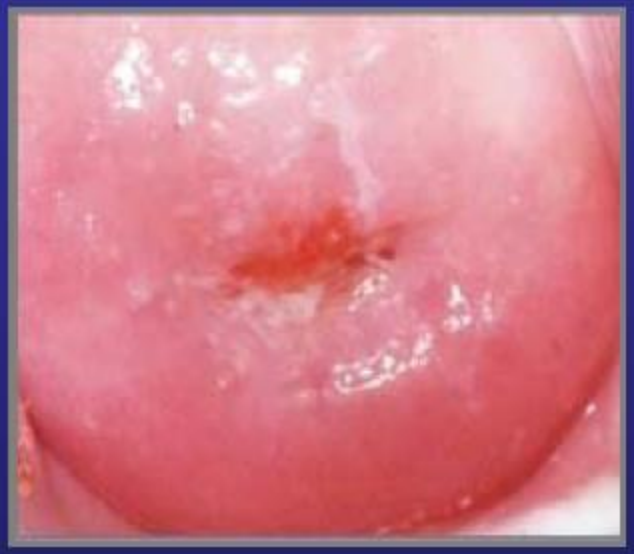
Images top left: Reprinted with permission from Dr. Ferenczy and top right: Reprinted with permission from NZ DermNet (www.dermnetnz.org). Bottom right: Reprinted with permission from Melbourne Sexual Health Centre (www.mshc.org.au).

- HPV 6 and 11 are responsible for >90% of anogenital warts.[1]
- Anogenital warts are common[2] and highly contagious[3]:
  - Based on National Health and Nutrition Examination Survey (NHANES) study, an estimated 4% of sexually active men 18 to 59 years of age have ever been diagnosed with genital warts.[2]
  - >75% of sexual partners develop warts when exposed.[3]
- Peak prevalence:[4]
  - Women 20 to 24 years of age (6.2/1,000 person-years).
  - Men 25 to 29 years of age (5.0/1,000 person-years).
- Clinically apparent in ~1% of sexually active US adult population.[5]

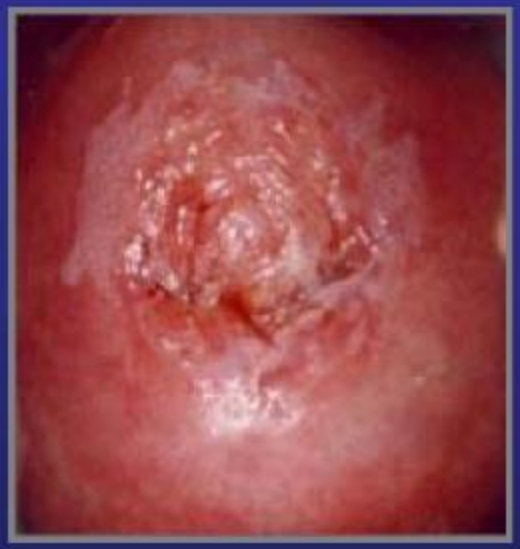
1. Gissmann L et al. *Proc Natl Acad Sci USA.* 1983;80:560-563. **2.** Dinh T-H et al. *Sex Transm Dis.* 2006;35(4):357–360. **3.** Soper DE. In: Berek JS, ed. *Novac's Gynecology.* 13th ed. 2002:453–470. **4.** Insinga RP et al. *Clin Infect Dis.* 2003;36:1397–1403. **5.** Koutsky L. *Am J Med.* 1997;102:3–8.

Cervical Intraepithelial Neoplasia (CIN)[1]

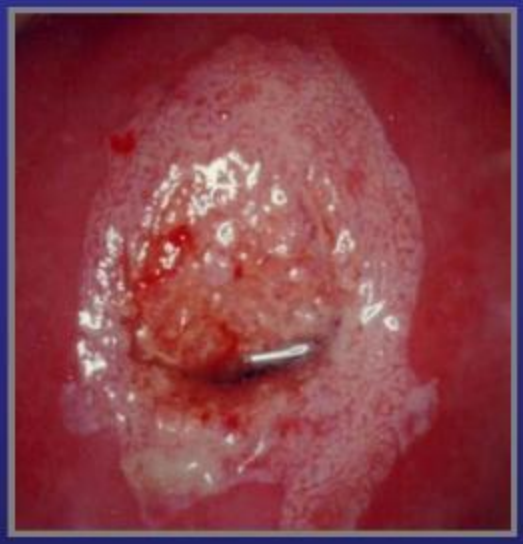
CIN 1



CIN 2



CIN 3



- CIN Stages[2]
  - CIN 1: Mild dysplasia
  - CIN 2: Moderate dysplasia
  - CIN 3: Severe dysplasia; includes carcinoma in situ (CIS)

1. Reprinted with permission from Dr. JW Sellors & Dr. R Sankaranarayanan. Sellors JW et al, eds. Lyon, France: International Agency for Research on Cancer;2003. *Colposcopy and Treatment of Cervical Intraepithelial Neoplasia. A Beginner's Manual.* Reprinted with permission of the International Agency for Research on Cancer, World Health Organization. 2. Bonnez W et al. In: Richman DD et al, eds. *Clinical Virology.* 2nd edition. American Society for Microbiology, Washington, NY. 2002:569--611.

Symptoms and Treatment of VIN

- HPV 16 and 18 contribute to 6.8% of VIN 1 and 76% to 86.6% of VIN 2/3 lesions.[1,2]
- Frequent symptoms are pruritus, vulval pain or discoloration, and vaginal discharge.[3]
- Symptoms may be present for a long time prior to diagnosis (median of 1 year).[3]
- Recommended treatment is surgery, including vulvectomy or wide local excision.[3,4]
  - Recurrence is likely when lesions are not completely excised.[4,5]
- Laser ablative techniques have had variable outcomes and can be associated with painful healing.[3,4]

VIN = vulvar intraepithelial neoplasia.

VIN 3

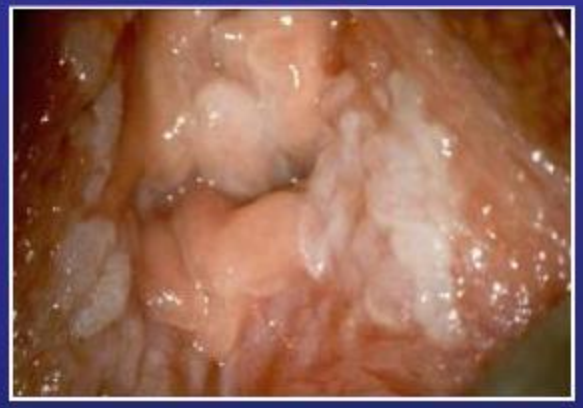


Photo courtesy of Dr. J Monsonego.

VIN 3

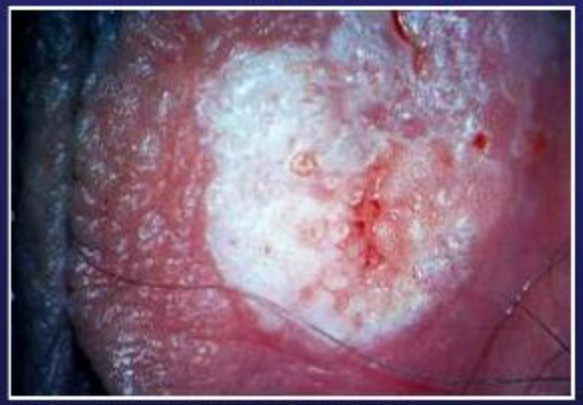


Photo courtesy of Dr. EJ Mayeaux.

1. Insigna RP et al. *Cancer Epidemiol Biomarkers Prev.* 2008;17:1611–1622. **2.** Hampl M et al. *Obstet Gynecol.* 2006;108:1361–1368. **3.** Herod JJ et al. *Br J Obstet Gynaecol.* 1996;103:446–452. **4.** Hatch KD. *Int J Gynaecol Obstet.* 2006;94(suppl 1):S36–S39. **5.** Jones RW et al. *Obstet Gynecol.* 2005;106:1319–1326.

HPV-associated conditions
HPV types 16, 18, 6, 11

- HPV 16, 18
  - Low/High grade intraepithelial neoplasias
  - Cervical cancers
  - Anal cancers
  - Vulvar/vaginal cancers
  - Penile cancers
  - Oropharyngeal cancers
- HPV 6, 11
  - Low grade intraepithelial neoplasias
  - Genital warts
  - Recurrent respiratory papillomatosis (RRP)

Clifford GM, BJ Ca 2003, Munoz Int J Cancer 2004; Brown J Clin Micro 1993; Carter Cancer Res 2001;
Clifford Cancer Epi Biomarkers Prev 2005; Gissman Proc Natl Acad Science 1983;
Kreimer Cancer Epidemiol Biomarkers Prev. 2005,
Insinga RP et al. American Journal of Obstetrics and Gynecology 2004

Preventing Cervical Cancer and Other HPV-Related Diseases

USPPI
Patient Information About GARDASIL

What is GARDASIL?

GARDASIL is a vaccine (injection/shot) that is used for girls and women 9 through 26 years of age to help protect against the following diseases caused by Human Papillomavirus (HPV):

- Cervical cancer
- Vulvar and vaginal cancers
- Anal cancer
- Genital warts
- Precancerous cervical, vaginal, vulvar, and anal lesions

GARDASIL is used for boys and men 9 through 26 years of age to help protect against the following diseases caused by HPV:

- Anal cancer
- Genital warts
- Precancerous anal lesions

Targeting a High Disease Burden With GARDASIL®

HPV Type	Approximate Disease Burden
16 and 18	• 70% of cervical cancer, AIS, CIN 3, VIN 2/3, and VaIN 2/3 cases • 50% of CIN 2 cases
6, 11, 16, and 18	• 35%–50% of all CIN 1, VIN 1, and VaIN 1 cases • 90% of genital warts cases

AIS = adenocarcinoma *in situ*
CIN = cervical intraepithelial neoplasia
VIN = vulvar intraepithelial neoplasia
VaIN = vaginal intraepithelial neoplasia

Additional Indications and Usage

- GARDASIL is indicated in boys and men 9 through 26 years of age for the prevention of anal cancer caused by HPV types 16 and 18 and the prevention of anal intraepithelial neoplasia (AIN) grades 1, 2, and 3 caused by HPV types 6, 11, 16, and 18.

- GARDASIL is indicated in girls and women 9 through 26 years of age for the prevention of anal cancer caused by HPV types 16 and 18 and the prevention of anal intraepithelial neoplasia (AIN) grades 1, 2, and 3 caused by HPV types 6, 11, 16, and 18.

HPV=human papillomavirus.

Efficacy: 100% Efficacious Against HPV 16- and 18-Related Cervical Cancer Precursors[1]

PPE-Combined Population; subjects were naïve to HPV Types 6, 11, 16, and/or 18

Combined Analysis

End Point: HPV 16/18-related	n	GARDASIL® or HPV 16 L1 VLP Cases*	n	Placebo Cases	Efficacy	95% CI
CIN 2/3 or AIS	8,487	0	8,460	53	**100%**	93–100
CIN 3 or AIS†‡	8,487	0	8,460	32	**100%**	88–100

- The efficacy of GARDASIL against HPV 16-, and 18-related VIN 2/3 or VaIN 2/3 was 100%.

*Analysis of CIN 2/3 and AIS endpoints included protocol 005.
†Defined by FIGO as Stage 0 cervical cancers; FIGO = International Federation of Gynecology and Obstetrics.
‡CIN 3 or AIS analysis was a secondary end point.
1. Data on file.

Efficacy Against HPV 6/11/16/18-Related Lesions[1]

PPE-Combined Population; subjects were naïve to HPV Types 6, 11, 16, and/or 18

Combined Analysis

End Point: HPV 6/11/16/18-related	GARDASIL® Cases	Placebo Cases	Vaccine Efficacy	95% CI
	n=7,858	n=7,861		
CIN or AIS	4	83	**95%**	87–99

End Point: HPV 6/11/16/18-related	GARDASIL Cases*	Placebo Cases*	Vaccine Efficacy	95% CI
	n=7,897	n=7,899		
Genital warts	1	91	**99%**	94–100

- The efficacy of GARDASIL against HPV 6-, 11-, 16-, and 18-related VIN 1 or VaIN 1 was 100%.

1. Data on file, MSD.

Selected Information About GARDASIL®[1]

- Indicated in girls and women 9 to 26 years of age for the prevention of cervical cancer, precancerous or dysplastic lesions, and genital warts caused by HPV Types 6, 11, 16, and 18.
- Contraindicated in individuals who are hypersensitive to the active substances or to any of the excipients of the vaccine.
- Vaccination with GARDASIL does not substitute for routine cervical cancer screening.
- Vaccination with GARDASIL may not result in protection in all vaccine recipients.
- Is not intended to be used for treatment of active genital warts; cervical cancer; CIN, VIN, or VaIN.
- Has not been shown to protect against diseases due to non-vaccine HPV types.

1. Data on file, MSD.

Vaccine-Related Experiences[1]

Injection site (1 to 5 days postvaccination)			
	GARDASIL® (N=5,088)	Placebo (Aluminum) (N=3,470)	Placebo (Saline) (N=320)
Pain	83.9%	75.4%	48.6%
Swelling	25.4%	15.8%	7.3%
Erythema	24.6%	18.4%	12.1%
Pruritus	3.1%	2.8%	0.6%

Systemic Adverse Event (1 to 15 days postvaccination)		
	GARDASIL (N=5,088)	Placebo (N=3,790)
Fever	10.3%	8.6%
Nausea	4.2%	4.1%
Dizziness	2.8%	2.6%

- Few subjects (0.1%) discontinued due to AEs.

The vaccine-related adverse experiences that were observed among recipients of GARDASIL were at a frequency of at least 1.0% and also at a greater frequency than that observed among placebo recipients.

1. Data on file, MSD.

Overall Conclusions for GARDASIL®

- Highly effective in preventing cervical cancer, CIN 2/3, AIS, and other anogenital diseases caused by HPV 6, 11, 16, and 18 in 16- to 26-year-old women naïve to the relevant HPV types
- Successful immunogenicity bridge between female adolescents and young adult women
  - Antibody response in 9- to 15-year-old females is higher, compared with response observed in young adult women (16–26 years old)
- Duration of efficacy is demonstrated between 2 and 4 years
- Favorable tolerability profile

Why Early Vaccination?

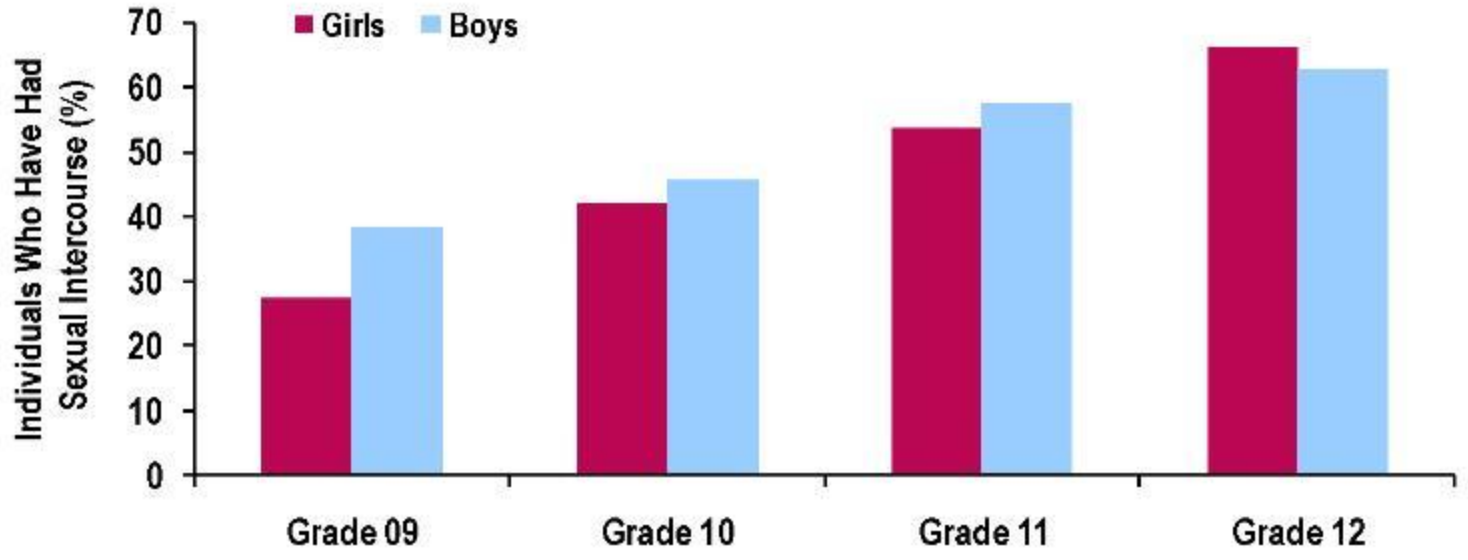
- Important to reach younger adolescents prior to exposure
- Adolescent females may have increased susceptibility to HPV infection[1-3]
- Timing opportunity: young children (9 to 12 years old) have more frequent contact with health care provider (pediatrician) than older adolescents (>13 years old)[4]
- Adolescents are sexually active[5]
  - Nationwide, 7.4% of the students had sexual intercourse for the first time before age 13 years.
  - Overall, the prevalence of female students having sexual intercourse before age 13 years was 4.2%.[5]

1. Kahn JA. *Curr Opin Pediatr*. 2001;13:303–309. 2. Rager KM, Kahn JA. *Curr Women Health Rep*. 2002;2:468–475. 3. ACOG Committee on Adolescent Health Care. Obstet Gynecol. 2004;104:891–898. 4. Oster NV, Phillips-Tangum CA, Averhoff F, et al. *J Am Board Fam Pract*. 2005;18:13–19. 5. Grunbaum JA, Kann L, Kinchen S, et al. *MMWR*. 2004;53(SS-2):1–96.

Sexual Activity Among US High School Students[1]

Centers for Disease Control and Prevention 2007 US Youth Risk Behavior Survey (N = 14,103)[1]

Percentage of US High School Students Who Have Had Sexual Intercourse[2]



7.1% of US adolescents reported sexual debut before age 13[1,2]

14.9% of US adolescents reported ≥ 4 lifetime sexual partners by Grade 12[1,2]

1. Eaton DK et al. *MMWR Surveill Summ.* 2008;57(SS04):1–131. **2.** Gavin L et al. *MMWR Surveill Summ.* 2009;58(SS06):1–58.

Facilitating Communication With Parents Through Shared Decision Making

- Initiate conversation about parental concerns or questions.[1]
- Provide relevant information about the clinical decision, alternatives, risks, and benefits.[2]
  - Education on the potential seriousness of HPV-related diseases.[3]
  - Discussion of the efficacy, safety, precautions, contraindications, and common side effects of the quadrivalent HPV vaccine.[3]
- Elicit information about beliefs, concerns, knowledge, and preferences.[2]
  - Be respectful of opinions, including those based on misinformation—people whose views are discussed are more likely to consider corrective information.[1]
- Enable the parent to feel empowered to make an informed decision.[1]
- Re-initiate conversation as needed.

1. Zimet GD. *J Adolesc Health.* 2005;37(suppl 6):S17–S23. **2.** Anhang R et al. *CA Cancer J Clin* 2004;54(5):248–259. **3.** Kahn JA et al. *Obstet Gynecol.* 2008;111 (5):1103-1110.

Limitations of Risk-Based Vaccination Strategies

- Risk-based vaccination strategy:
  - Using behavioral risk factors (primarily sexual history) to identify populations most suitable for HPV vaccination.[1]
- Study conclusion: risk stratification is not a viable strategy for HPV vaccination of young adults.[1]
  - An estimated 25% to 80% of eligible young women who could benefit from vaccination would be excluded using a risk-factor–based approach.

"[It is not possible for a clinician to assess the extent to which sexually active persons would benefit from vaccination, and the risk for HPV infection might continue as long as persons are sexually active."[2]

— ACIP

ACIP= Advisory Committee on Immunization Practices.

1. Dempsey AF et al. *Vaccine.* 2008;26(8):1111–1117. **2.** Centers for Disease Control and Prevention (CDC). *MMWR Recomm Rep.* 2007;56(RR-2):1–24.

Perceived Challenges to Adult Vaccination: Survey[1,a]

Patient Reasons

- *"Doctor hasn't told me I need it."*
- Not knowing when to get it.
- The belief that a healthy person doesn't need it.
- Financial concerns were not a deterrent for most.

Health Care Provider Perceptions

- Side effects.
- Dislike of needles.
- Lack of insurance coverage.
- Lack of knowledge about disease prevention.

Most patients indicated that they were likely to receive a vaccination if their health care provider recommended it.

[a]A recent survey was conducted to identify the reasons adult patients may decide to **NOT** receive vaccinations and health care providers' perceptions regarding patients' **NOT** being vaccinated.
Consumers (N = 2,002) and health care providers (N = 200) completed structured telephone interviews, e-mails, or faxes emphasizing tetanus, influenza, and pneumococcal vaccines.

1. Johnson DR et al. *Am J Med.* 2008;121(7 suppl 2):S28–S35.

Summary

- HPV infection is common in both the United States and worldwide.
- Virtually all cases of cervical cancer are linked to high-risk HPV types.
- HPV is easily transmitted and often asymptomatic.
  - HPV depends on the differentiation of the epithelium to regulate its replication and complete its life cycle.
  - The natural immune response to cervical HPV infection is slow and weak because of the ability of HPV to evade immune responses.

Conclusions

- Cancers associated with HPV include cervical, vaginal, vulvar, anal and oropharyngeal cancers.
- "Head and neck" cancers have an important burden but the oropharynx is only site strongly associated with HPV.
- Cancer Registries and data are a valuable resource.
  - Lag period of 2-3 years
- There are approximately 25,000 HPV-associated cancers and approximately 22,000 HPV 16/18-associated cancers.
- There is a trend of increasing oropharyngeal cancers, especially in men, and anal cancers, in men and women.

Indications and Usage

GARDASIL® [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant]	*Cervarix*® [Human Papillomavirus Bivalent (Types 16 and 18) Vaccine, Recombinant]
Girls and Women GARDASIL is a vaccine indicated in girls and women 9 through 26 years of age for the prevention of the following diseases caused by HPV types included in the vaccine: •Cervical, vulvar, and vaginal cancer caused by HPV Types 16 and 18 •Genital warts (condyloma acuminata) caused by HPV Types 6 and 11 And the following precancerous or dysplastic lesions caused by HPV Types 6, 11, 16, and 18: •Cervical intraepithelial neoplasia (CIN) grade 2/3 and cervical adenocarcinoma in situ (AIS) •CIN grade 1 •Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3 •Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3 **Boys and Men** GARDASIL is indicated in boys and men 9 through 26 years of age for the prevention of genital warts (condyloma acuminata) caused by HPV Types 6 and 11.	**Girls and Women** *Cervarix* is a vaccine indicated for the prevention of the following diseases caused by oncogenic HPV Types 16 and 18: •Cervical cancer •CIN grade 2 or worse and AIS, and •CIN grade 1 *Cervarix* is approved for use in females 10 through 25 years of age.

Indications and Usage (*cont*): Limitations of Use and Effectiveness

GARDASIL® [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant]	*Cervarix*® [Human Papillomavirus Bivalent (Types 16 and 18) Vaccine, Recombinant]
• GARDASIL does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. • GARDASIL has not been demonstrated to protect against disease from vaccine and non-vaccine HPV types to which a person has previously been exposed through sexual activity. • GARDASIL is not intended to be used for treatment of active external genital lesions; cervical,vulvar, and vaginal cancers; CIN, VIN; or VaIN. • GARDASIL has not been demonstrated to protect against diseases due to HPV types not contained in the vaccine. • Not all vulvar and vaginal cancers are caused by HPV, and GARDASIL protects only against those vulvar and vaginal cancers caused by HPV 16 and 18. • GARDASIL does not protect against genital diseases not caused by HPV. • Vaccination with GARDASIL may not result in protection in all vaccine recipients.	• *Cervarix* does not provide protection against disease due to all HPV types. • *Cervarix* has not been demonstrated to provide protection against disease from vaccine and non-vaccine HPV types to which a woman has previously been exposed through sexual activity. • Females should continue to adhere to recommended cervical cancer screening procedures. • Vaccination with *Cervarix* may not result in protection in all vaccine recipients.